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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/060,294	04/15/1998	MARTIN ROLAND JENSEN	P60953US1	9443

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JACOBSON PRICE
HOLMAN AND STERN
THE JENIFER BUILDING
400 SEVENTH STREET NW
WASHINGTON, DC 20004

EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/060,294	JENSEN ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *91-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *97* is/are rejected.

7)☒ Claim(s) *91-96* is/are objected to.

8)☒ Claim(s) *91-97* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948).
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The finality of the rejection of the last Office action is withdrawn in order to make a new grounds of rejection.

The amendment filed 12/28/2004 has been entered. Claims 91-97 are pending.

Applicant's elected group I in the paper filed 10/21/2003. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's elected with traverse the species E/F loop substitution in the paper filed 10/21/2003. The traversal was on the ground(s) that the substitution in the E strand and in the E/F connecting loop species and the substitution in the E strand and in the E/F and D/E connecting loop species should also be examined with the elected species. This was found persuasive. The requirement was still deemed proper and was therefore made FINAL. Claims 82-84, 86, 98-103, 107-109, 111, 115, 116, 123, 125-127, 128, 130 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species or invention, there being no allowable generic or linking claim. Claims 91-97 are being examined to the extent that they read upon the elected species. Applicant timely traversed the restriction (election) requirement in the paper filed 10/21/2003.

New Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 103

Claim 97 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mouritsen (AV, cited by Applicants) in view of {Pennica (BP, cited by Applicants), Shirai (BN, cited by Applicants), or Wang (BL, cited by Applicants)}, and further in view of Jones (BF, cited by Applicants), and further in view of Panina-Bordigon (BO, cited by Applicants) and Le (U. S. Patent No. 5656272) as applied to claim 77 in the last Office action (mailed 10/05/2004), and further in view of Hellman (N), Cox (AW, cited by Applicants), and Cooke (U).

Mouritsen in view of {Pennica, Shirai, or Wang}, and further in view of Jones, and further in view of Panina-Bordigon and Le teach a modified human TNFα molecule capable of raising neutralizing antibodies towards wild-type human TNFα following administration of said modified TNFα molecule to a human host, wherein at least one segment of the human TNFα molecule has been substituted by at least one peptide containing an immunodominant T cell epitope or a truncated form of said molecule containing an immunodominant T-cell epitope and one or both flanking regions of the human-TNFα molecule comprising at least one TNFα B cell epitope, wherein the substitution is introduced in any one of the strands of the front β-sheet, in any one of the connecting loops or in any one of the B', I, or D strands of the back β-sheet, or in any one of the connecting loops in any one of the B', I, or D strands of the back β-sheet, and which substitution leads to inactivation of the biological activity of human TNFα and which substitution essentially ensures preservation of the β-sheet structures of the B and G strands, as discussed in the last Office action. Mouritsen in view of {Pennica, Shirai, or Wang}, and further

in view of Jones, and further in view of Panina-Bordigon and Le do not teach dimers, oligomers, or multimers of a modified human TNFα molecule.

Hellman teaches a vaccine containing a protein having the entire amino acid sequence of the constant CH2-CH3 domains of the epsilon chain of the IgE molecule or a structurally stable unit of said amino acid sequence (Abstract) and a multimerized form (paragraph bridging pages 4-5) wherein the amino acid sequence (the entire sequence or part thereof) of the protein has been polymerized to a form containing two or more repeating units thereof (paragraph bridging pages 5-6).

Cox teaches an LHRH based vaccine comprising a recombinant polypeptide comprising an amino acid sequence corresponding to LHRH and one or more T-cell epitopes (page 3, full paragraph 2). The LHRH amino acid sequence may be represented once in the polypeptide or as tandem or multiple repeats (page 4, lines 15-18).

Cooke discloses that studies of self-nonself discrimination have confirmed the clonal selection theory, which hypothesized that foreign antigens provoke immunity by triggering clonal expansion and differentiation of Ag-binding B and T lymphocytes, whereas self-Ags induce tolerance by triggering elimination or inactivation of self-reactive cells. Understanding the molecular basis for these cellular decisions will be important for controlling immunogenicity or tolerogenicity of vaccines (page 425, paragraph bridging left and right columns). Tolerant B cells remain responsive to T cell-derived signals, but exhibit a proximal block in B cell signaling after Ag biding that precludes effective collaboration with T cells. Moreover, the sIg signaling block can be partially overcome by very extensive receptor cross-linking, and this markedly restores collaboration with Th cells. These findings demonstrate a pivotal role for sIg signaling

in guiding T cell-dependent Ab responses (page 426, paragraph bridging left and right columns). A highly multivalent form of Ag can restore sIg signaling in tolerant B cells (page 434, left column) and this markedly restored their ability to mount an Ab response in the presence of activated Th cells (page 435, left column, full paragraph 1).

Hellman, Cox, and Cooke do not teach a dimers, oligomers, or multimers of a modified human TNFα molecule. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make a modified TNFα molecule, as taught by Mouritsen in view of {Pennica, Shirai, or Wang}, and further in view of Jones, and further in view of Panina-Bordigon and Le, and to modify that teaching by making dimers, oligomers, or multimers of a modified TNFα molecule, as taught by Hellman, Cox, and Cooke, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because the prior recognizes making multimeric vaccines and because a multivalent form of an Ag can restore sIg signaling in tolerant B cells and markedly restore their ability to mount an Ab response in the presence of activated Th cells. The invention is prima facie obvious over the prior art.

Claim Objections

Claims 91-96 are objected to because of the following informalities: claim 91 contains a typographical error wherein the clause "wherein the inserted ... and SEQ ID NO: 20" is duplicated. Claims 92-96 are objected to because they depend from claim 91 and therefore also share this error. Appropriate correction is required.

Conclusion

Claims 91-96 are allowable if the objection is overcome.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300 CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
MARCH 7, 2005